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FAX COVER

Date: March 9, 2005 **Number of pages** (including cover) 7

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Telephone No.:
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Serial No: 09/347,311
Conf. No.: 3674
Filing Date: July 2, 1999
Title: CHARACTERISATION OF GENE FUNCTION USING DOUBLE STRANDED RNA INHIBITION
Fax Number: 571-273-0739

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ORIGINAL DOCUMENTS SENT: __ 1st Class Mail _ Overnight Mail __ Air Mail X Not Sent

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Typed or Printed Name of Person: June M. Watson Date: March 9, 2005
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DRAFT CLAIMS for USSN 09/347,311

[D0590.70003US00 -- P98/003US]

1. (Currently amended) A method of identifying DNA responsible for conferring a phenotype of a *C. elegans* cell or *C. elegans* organism, which method comprises

a) constructing a cDNA or genomic library of the DNA of said *C. elegans* cell or *C. elegans* organism in a vector in an orientation relative to a promoter(s) that initiates transcription of said cDNA or DNA to double stranded (ds) RNA upon binding of a transcription factor to said promoter(s),

b) introducing said ~~library~~ dsRNA into ~~one or more~~ a plurality of said *C. elegans* cells or *C. elegans* organisms ~~comprising said transcription factor~~, and

c) identifying a phenotype of said *C. elegans* cell or *C. elegans* organism comprising a member of said library and identifying the DNA or cDNA from said library responsible for conferring said phenotype.

93. (New) The method of claim 1, wherein the step of introducing said dsRNA comprises feeding micro-organisms comprising said dsRNA to said *C. elegans* organisms.

94. (New) The method of claim 93, wherein the micro-organisms are bacteria or yeast.

95. (New) The method of claim 94, wherein the bacteria are *E. coli*.

96. (New) The method of claim 93, wherein the library is transformed in the micro-organisms.

2. (Original) A method according to claim 1 wherein said library is organised into hierarchical pools prior to step b).

3. (Currently amended) A method of assigning function to a known DNA sequence which method comprises

a) identifying a homologue(s) of said known DNA sequence in a *C. elegans* cell or *C. elegans* organism,

b) isolating the relevant DNA homologue(s) or a fragment thereof from said *C. elegans* cell or *C. elegans* organism,

c) cloning said homologue or fragment thereof into a vector in an orientation relative to a promoter(s) that initiates transcription of dsRNA from said DNA homologue or fragment upon binding of a transcription factor to said promoter(s),

d) transforming micro-organisms with said vector,

~~d)~~e) ~~introducing said vector into~~ feeding said micro-organisms to said ~~*C. elegans* cell or~~ *C. elegans* organisms ~~organism from step a) comprising said transcription factor~~, and

~~e)~~f) identifying the phenotype of said ~~*C. elegans* cell~~ or *C. elegans* organisms ~~organism~~ compared to wild type.

97. (New) The method of claim 3, wherein the micro-organisms are bacteria or yeast.

98. (New) The method of claim 97, wherein the bacteria are *E. coli*.

4. (Currently amended) A method according to any of claims 1, ~~or~~ 3 or 93 wherein said DNA library, homologue or fragment is cloned in a sense and an antisense direction relative to said promoter.

5. (Currently amended) A method according to any of claims 1, ~~or~~ 3 or 93 wherein said DNA library, homologue or fragment is cloned between two promoters capable of producing dsRNA from said DNA library, homologue or fragment upon binding of said transcription factor to said promoters.

6. (Currently amended) A method according to any of claims 1, ~~or~~ 3 or 93 wherein said cell is adapted to express said transcription factor.

7. (Currently amended) A method according to any of claims 1, ~~or~~ 3 or 93 wherein said DNA library, homologue or fragment is constructed in a suitable vector which comprises a sequence of nucleotides encoding said transcription factor operably linked to a promoter.

8. (Currently amended) A method according to any of claims 1, ~~or~~ 3 or 93 wherein said transcription factor is encoded by a further vector independent of the vector including said DNA library, DNA homologue or fragment and which sequence encoding said transcription factor is operably linked to a promoter.

9. (Previously presented) A method according to claim 7 wherein said transcription factor comprises any of T7, T3 or SP6 polymerase.

10. (Previously presented) A method according to claim 7 wherein said promoter comprises any of let 858, SERCA, UL6, myo 2 or myo 3.

11. (Previously presented) A method according to claim 7, wherein said vector comprises a selectable marker.

12. (Previously presented) A method according to claim 11 wherein said selectable marker comprises a nucleotide sequence capable of inhibiting or preventing expression of a gene in said *C. elegans* cell or *C. elegans* organism and which gene is responsible for conferring a second phenotype.

13. (Previously presented) A method according to claim 12 wherein said nucleotide sequence comprises a sequence which is a part of or identical to said gene conferring said second phenotype, and which nucleotide sequence is itself oriented relative to a promoter(s) that initiates transcription of double stranded RNA upon binding of a transcription factor to said promoter(s).

14. (Previously presented) A method according to claim 12 wherein said nucleotide sequence is a part of or identical to said gene conferring said second phenotype, and which

nucleotide sequence permits integration of said vector by homologous recombination in the genome of said *C. elegans* cell or *C. elegans* organism wherein said nucleotide sequence does not express said gene sequence.

15. (Original) A method according to claim 14 wherein said nucleotide sequence comprises stop codons sufficient to prevent translation of said nucleotide sequence following its integration into said genome.

16. (Canceled)

17. (Currently amended) A method according to any of claims 1, ~~or~~ 3 or 93 wherein said *C. elegans* cell is contained in an organism or an embryo thereof.

18. (Currently amended) A method according to any of claims 1, ~~or~~ 3 or 93 wherein said promoters are T7 promoters.

19. (Previously presented) A method according to claim 12 wherein said known gene sequence comprises a sup 35 gene or a fragment thereof which is selectable by identifying offspring growing at a temperature above 25°C following introduction of said vector in the genome of a pha I et123ts mutant *C. elegans* worm.

20. (Currently amended) A method according to any of claims 1, ~~or~~ 3 or 93 further comprising contacting said *C. elegans* cell or *C. elegans* organism with a compound for screening for a phenotype.

21. (Currently amended) A method according to any of claims 1, ~~or~~ 3 or 93 wherein said transcription factor is inducible.

22.-37. (Canceled)

38. (Previously presented) A method of validating clones identified in yeast two hybrid vector experiments which method comprises

a) providing a construct including the DNA encoding the protein identified in the two hybrid vector experiment, which construct is such that said DNA is orientated relative to a promoter(s) that initiates transcription of said DNA to double stranded RNA upon binding of a transcription factor to said promoter(s),

b) transforming a *C. elegans* cell or *C. elegans* organism comprising said transcription factor with said construct, and

c) identifying a phenotypic change in said *C. elegans* cell or *C. elegans* organism when compared to a wild type.

39. (Original) A method according to claim 38 wherein said DNA sequence is provided between two promoters capable of initiating transcription of the DNA sequence to dsRNA upon binding of the transcription factor to said promoters.

40. (Original) A method according to claim 38 wherein said DNA is provided in a sense and an antisense orientation relative to said promoter such that binding of the transcription factor to said promoter initiates transcription of dsRNA from said DNA.

41. (Previously presented) A method according to claim 38 wherein said transcription factor is inducible in said *C. elegans* cell.

42. (Previously presented) A method according to claim 38 wherein said promoter is a phage polymerase promoter and said transcription factor is a RNA polymerase.

43. (Original) A method according to claim 42 wherein said polymerase is any of T7 RNA polymerase, T3 RNA polymerase or SP6 RNA polymerase.

44. (Original) A method according to claim 43 wherein said promoters comprise any of T7, T3 or SP6 promoter.

45. (Previously presented) A method according to claim 38 wherein said construct is such that it may be used in yeast two hybrid experiments.

46. (Canceled)

47. (Previously presented) A method according to claim 38 wherein said cell is part of an organism or an embryo thereof.

48.-91. (Canceled)

92. (Previously presented) A method according to claim 20 wherein said phenotype is resistance or sensitivity to said compound when compared to the wild type *C. elegans* cell or *C. elegans* organism.